

CAS ONLINE PRINTOUT

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(FILE 'HOME' ENTERED AT 13:50:48 ON 12 DEC 2002)

FILE 'REGISTRY' ENTERED AT 13:51:11 ON 12 DEC 2002

L1 STRUCTURE UPLOADED

L2 50 S L1

L3 17524 S L1 FUL

FILE 'CAPLUS' ENTERED AT 13:51:58 ON 12 DEC 2002

L4 3315 S L3

L5 73675 S DIABETE?

L6 720 S L5 AND L4

L7 73653 S DIABETES

L8 720 S L7 AND L4

L9 24101 S L7/TI

L10 222 S L9 AND L4

FILE 'REGISTRY' ENTERED AT 14:00:47 ON 12 DEC 2002

L11 STRUCTURE UPLOADED

L12 10 SEARCH L11 SSS SUB=L3 FUL

FILE 'REGISTRY' ENTERED AT 14:04:00 ON 12 DEC 2002

L13 2 S L12

FILE 'CAPLUS' ENTERED AT 14:04:52 ON 12 DEC 2002

=> s l12

L14 4 L12

=> s l14 and l7

L15 4 L14 AND L7

=> d bib abs hitstr 1-4

L15 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 2002:185699 CAPLUS

DN 136:247571

TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as inhibitors of cytokines or cyclooxygenase

IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi, Partha

PA USA

SO U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 785,554.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032225	A1	20020314	US 2001-843167	20010427
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002025975	A1	20020228	US 2001-785554	20010220
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

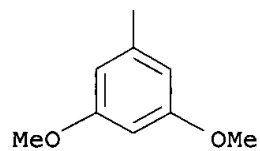
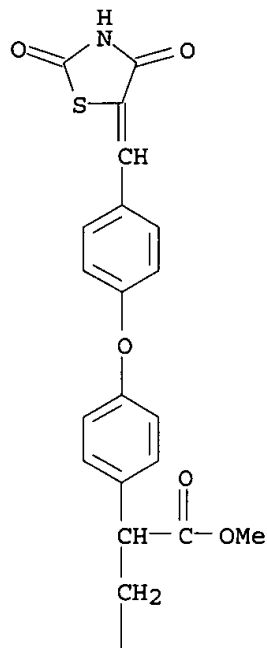
compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Thus, To a mixt. of 3,5-dimethoxybenzaldehyde (500 g) and p-hydroxyphenylacetic acid (457 g) was added acetic anhydride (1 L) and triethylamine (420 mL) and the nonhomogeneous mixt. on heating became homogeneous at 70.degree. and stirred at 130-140.degree. for 6 h to give 47% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid (II) (428 g). II (427.5 g) was suspended in 3 L methanol, treated with 100 mL concd. H2SO4, and heated at reflux for 20 h under Ar to give 97% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid Me ester (III). III (433 g) was dissolved in 1.6 L DMF, treated with 60.4 g NaH (50% in oil) and the with 185 mL p-fluorobenzaldehyde, and heated at 180.degree. for 18 h to give 77% 3-(3,5-dimethoxyphenyl)-2-[4-(4-formylphenoxy)phenyl]acrylic acid Me ester which (352 g), 2,4-thiazolidinedione 98.6, benzoic acid 134, and piperidine 107.4 g were heated in 2.5 L toluene at reflux with continuous removal of H2O through Dean-Stark app. to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid Me ester (IV). IV (30 g) was hydrogenated over 15 g 10% Pd-C in 900 mL dioxane in a Parr app. at 60 Psi for 24 h, followed by adding 15 g 10% Pd-C and continuing the hydrogenation for another 24 h to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylic acid Me ester (V). When V was orally administered to ob/ob mice with a single oral dose (50 mg/kg body wt.), there was a 62 % drop in blood glucose level and, similar to db/db mice, there was no significant increase in body wt. between the control and the treatment groups. This was in contrast to treatment of diabetic animals by thiazolidinedione type compds. which are known to be assocd. with increase in body wt.

IT **380881-47-0P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]propionic acid methyl ester **380881-49-2P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid **380881-51-6P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid methyl ester **380881-53-8P**, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]propionic acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

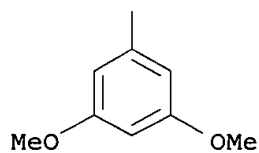
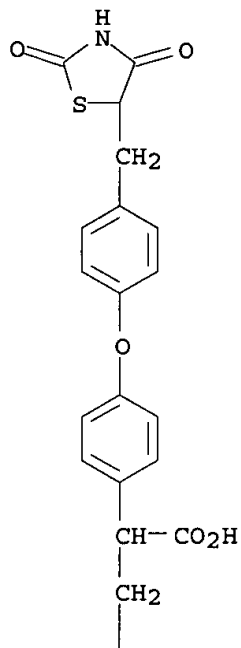
(prepn. of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 380881-47-0 CAPLUS

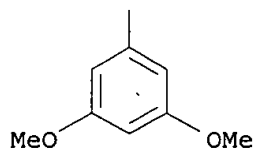
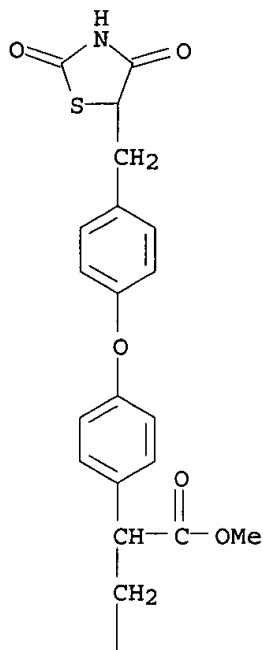
CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



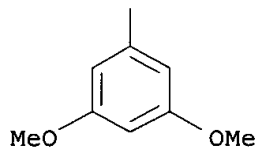
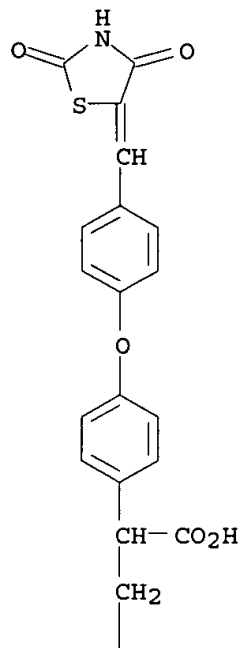
RN 380881-49-2 CAPLUS
 CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)



RN 380881-51-6 CAPLUS
 CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI)
 (CA INDEX NAME)



RN 380881-53-8 CAPLUS
CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)



L15 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 2001:923567 CAPLUS

DN 136:37596

TI Preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compounds as antidiabetics or antiinflammatories

IN Neogi, Partha; Nag, Bishwajit; Medicherla, Satyanarayana; Dey, Debendranath

PA Calyx Therapeutics, Inc., USA

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

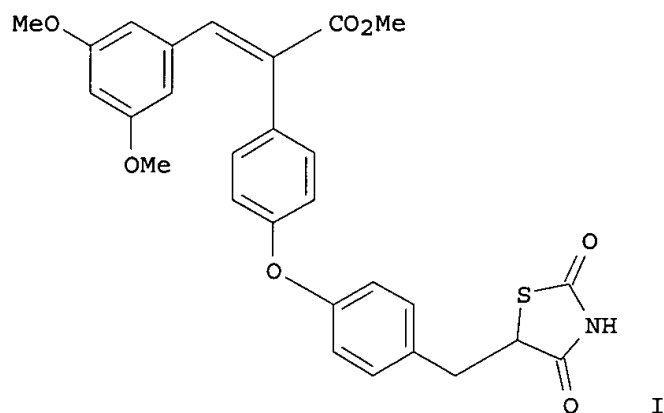
LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

CAS ONLINE PRINTOUT

	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
	BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US	2002025975 A1 20020228 US 2001-785554 20010220
US	2002032225 A1 20020314 US 2001-843167 20010427
AU	2001066670 A5 20011224 AU 2001-66670 20010605
PRAI	US 2000-591105 A2 20000609
	US 2001-785554 A2 20010220
	US 2001-843167 A2 20010427
	US 1998-74925 A2 19980508
	US 1999-287237 A2 19990406
WO	2001-US17950 W 20010605
OS	MARPAT 136:37596
GI	



AB Novel diphenylethylene compds. and derivs. thereof contg. thiazolidinedione or oxazolidinedione moieties are provided which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II **diabetes**. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, (I) was prepd. in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid followed by esterification and etherification with 4-fluorobenzaldehyde and condensation with 2,4-thiazolidinedione and hydrogenation of the ylidene double bond. Oral administration of I to obese mice caused a 62% drop in blood glucose level. The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis.

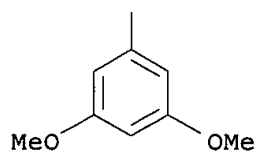
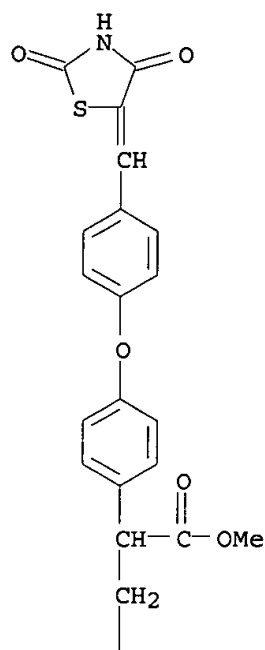
IT **380881-47-0P 380881-49-2P 380881-51-6P 380881-53-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

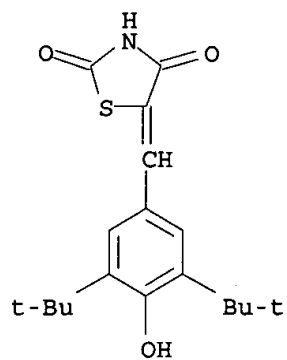
(prepn. and activity of diphenylethylene thiazolidinedione or oxazolidinedione compds. as antidiabetics or antiinflammatories)

RN 380881-47-0 CAPLUS

CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



RN 380881-49-2 CAPLUS
 CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)



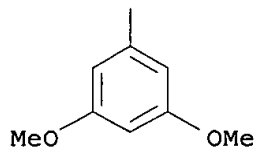
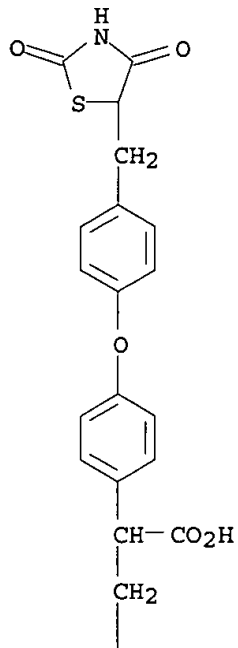
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN 2,4-Thiazolidinedione, 5-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]- (9CI) (CA INDEX NAME)

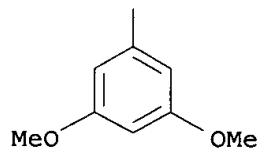
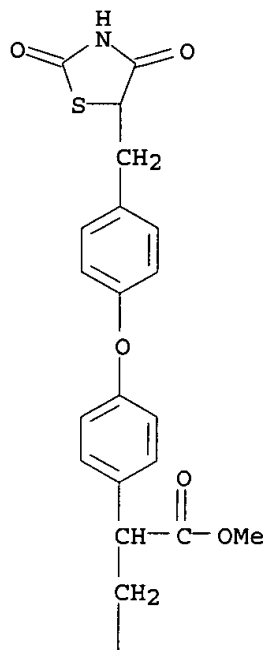
OTHER NAMES:

CN 5-(3,5-Di-tert-butyl-4-hydroxybenzylidene)thiazolidine-2,4-dione

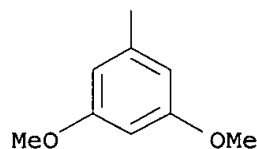
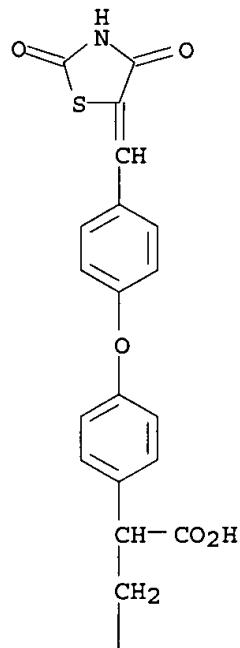
CN CI 987



RN 380881-51-6 CAPLUS
CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI)
(CA INDEX NAME)



RN 380881-53-8 CAPLUS
CN Benzenepropanoic acid, .alpha.-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)



L15 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1996:537366 CAPLUS
DN 125:195674
TI Preparation of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline derivatives having
blood sugar-lowering and aldose reductase-inhibiting activity
IN Myaoka, Shozo; Sato, Hiroko; Matsushima, Hiroaki; Sugizaki, Myoshi
PA Terumo Corp, Japan
SO Jpn. Kokai Tokkyo Koho, 33 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	JP 08143566	A2	19960604	JP 1994-291053	19941125
OS	MARPAT 125:195674				
GI					

AB The title compds. [I; R3, R4 = H, halo, lower alkyl, lower alkoxy, haloalkyl; R1, R2 = R5-CO2R6, CH2C6H4-A-T, (CH2)m-B-T; wherein R5 = C1-3 alkylene; R6 = H, C1-8 alkyl; A = CH2, 1,2-, 1,3-, or 1,4-NHSO2C6H4CH2, -CH2CH2C6H4CH2, or -CH:CHC6H4CH2; T = heterocyclyl having weakly acidic H; m = 1-7; B = NHSO2-C6H4-CH2], which are useful for the treatment of **diabetes** complications such as cataract, retinopathy, or nerve or kidney disorders, are prepd. Thus, Et 2,4-dioxo-2H-3,1-benzoxazine-1(4H)-acetate, 4-nitrobenzyl amine hydrochloride, and Et3N were suspended in toluene and stirred at 100.degree. for 2.5 h to give Et [2-[N-(4-nitrobenzyl)carbamoyl]phenylamino]acetate, which was cyclocondensed with 1,1'-carbonyldiimidazole at 130.degree. for 2 h to I (R1 = 4-nitrobenzyl, R2 = CH2CO2Et, R3 = R4 = H), diazotized with NaNO2 in HBr/aq. acetone at 5.degree., and coupled with Et acrylate in the presence of Cu2O at 30.degree. to give I (R1 = Q, R2 = CH2CO2Et, R3 = R4 = H). The latter compd. was cyclocondensed with thiourea in the presence of AcONa in ethanol under reflux for 6 h to I (R1 = Q1, wherein Z = NH, R2 = CH2CO2Et, R3 = R4 = H), which was hydrolyzed in 2 N aq. HCl under reflux to give I (R1 = Q1, wherein Z = O, R2 = CH2CO2Et, R3 = R4 = H) and I (R1 = Q1, wherein Z = O, R2 = CH2CO2H, R3 = R4 = H). I (R1 = Q2, R2 = CH2CO2H, R3 = 7-Cl, R4 = H) and I (R1 = Q3, R2 = CH2CO2H, R3 = R4 = H) in vitro showed IC50 of 3.34 .times. 10-8 and 2.13 .times. 10-6 M, resp., against aldose reductase, and at 100 mg/kg/day p.o. for 2 days in vivo lowered blood sugar by 13 and 36%, resp.

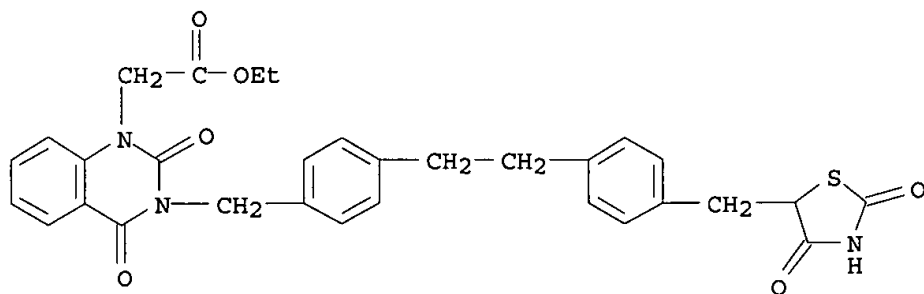
IT 180632-29-5P 180632-30-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of dioxotetrahydroquinazoline derivs. having blood sugar-lowering and aldose reductase-inhibiting activity for treating **diabetes** complications)

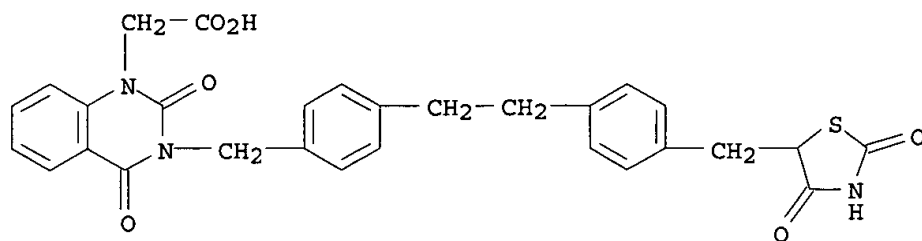
RN 180632-29-5 CAPLUS

CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 180632-30-8 CAPLUS

CN 1(2H)-Quinazolineacetic acid, 3-[[4-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]phenyl]methyl]-3,4-dihydro-2,4-dioxo- (9CI) (CA INDEX NAME)



L15 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 1992:255519 CAPLUS

DN 116:255519

TI Novel thiazolidine-2,4-diones as potent euglycemic agents.

AU Hulin, Bernard; Clark, David A.; Goldstein, Steven W.; McDermott, Ruth E.; Dambek, Paul J.; Kappeler, Werner H.; Lamphere, Charles H.; Lewis, Diana M.; Rizzi, James P.

CS Pfizer Inc., Groton, CT, 06340, USA

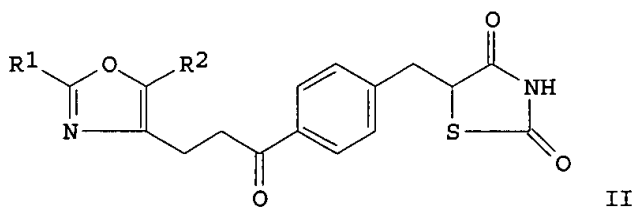
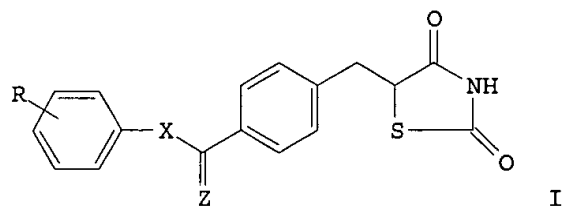
SO Journal of Medicinal Chemistry (1992), 35(10), 1853-64

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

GI



AB A new series of thiazolidine-2,4-diones I [R = H, Z = O, X = (CH₂)_n, (n = 1, 2, 3), OCH₂, CH:CH; R = 4-PhCH₂O, 4-Ph, 2-MeO, 4-MeO, Z = O, X = CH₂CH₂; R = H, Z = H₂ or H,OH, X = CH₂CH₂; R = 4-PhCH₂O, 2-MeO, 2-Cl, 2-CF₃, 2-PhCH₂, 3-Cl, 4-Br, 4-EtO₂C, 4-Ph, 2-HO, 2-Me, 4-MeOCH₂, 4-MeO, 4-Me₂N, Z = O, X = CH:CH] was obtained by replacing the ether function of englitazone with various functional groups, i.e., a ketone, alc., or olefin moiety. These compds. lower blood glucose levels in the genetically obese and insulin-resistant ob/ob mouse. Appending an oxazole-based group at the terminus of the chain provided highly potent compds., e.g. II [R₁ = Ph, 4-MeC₆H₄, R₂ = Me, H; R₁ = 4-MeOC₆H₄, 4-CF₃C₆H₄, 4-HOC₆H₄, 3,5,4-Me₂(MeO)C₆H₂, 3,5,4-Me₂(HO)C₆H₂, 2-furyl, 2-(5-methylfuryl), 2-HSC₆H₄, 2-naphthyl, R₂ = Me].

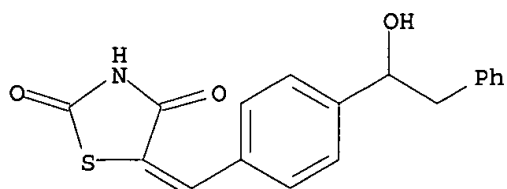
IT 141200-90-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with thiazolidinedione)

RN 141200-90-0 CAPLUS

CAS ONLINE PRINTOUT

CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methylene]-
(9CI) (CA INDEX NAME)



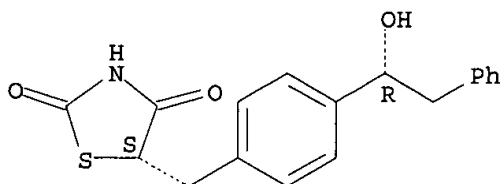
IT 141200-92-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and conjugate redn of, in prepn. of euglycemics)

RN 141200-92-2 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methyl]-,
(R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



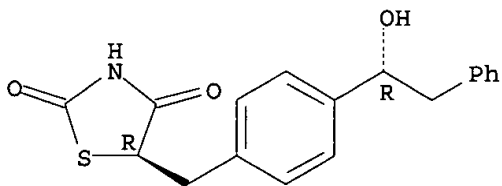
IT 141200-91-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and conjugate redn. of, in prepn. of euglycemics)

RN 141200-91-1 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-(1-hydroxy-2-phenylethyl)phenyl]methyl]-,
(R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

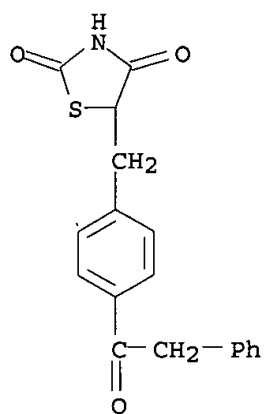


IT 141199-89-5P

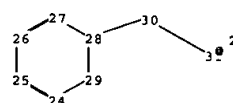
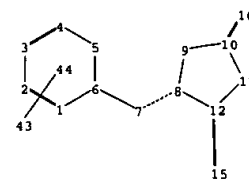
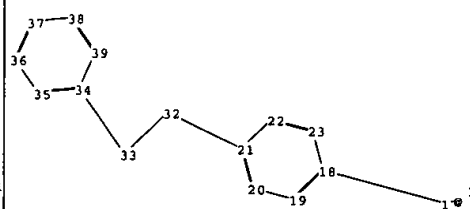
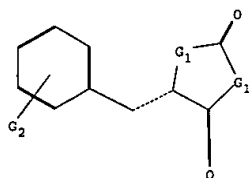
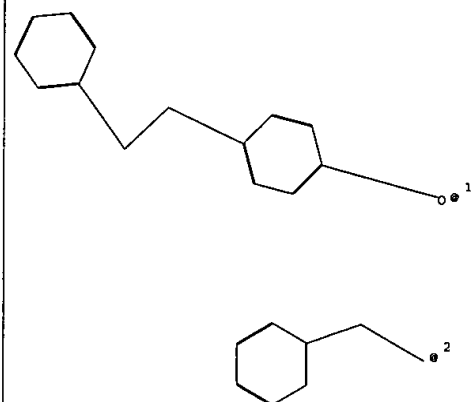
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and euglycemic activity of)

RN 141199-89-5 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-(phenylacetyl)phenyl]methyl]- (9CI) (CA
INDEX NAME)



=>



chain nodes :

7 15 16 17 30 31 32 33 43

ring nodes :

1 2 3 4 5 6 8 9 10 11 12 18 19 20 21 22 23 24 25 26 27 28 29 34 35
36 37 38 39

chain bonds :

6-7 7-8 10-16 12-15 17-18 21-32 28-30 30-31 32-33 33-34

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-12 9-10 10-11 11-12 18-19 18-23 19-20 20-21
21-22 22-23 24-25 24-29 25-26 26-27 27-28 28-29 34-35 34-39 35-36 36-37 37-38
38-39

exact/norm bonds :

6-7 7-8 8-9 8-12 9-10 10-11 10-16 11-12 12-15 17-18 21-32 28-30 30-31 32-33
33-34

normalized bonds :

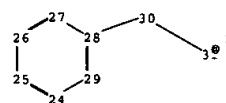
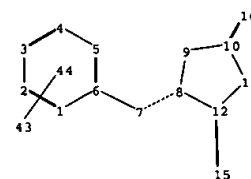
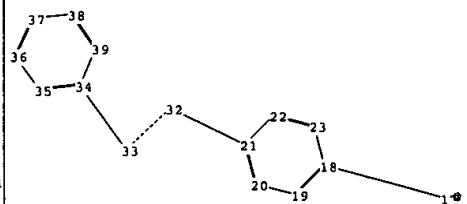
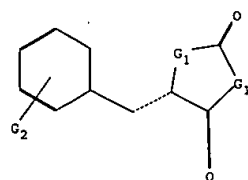
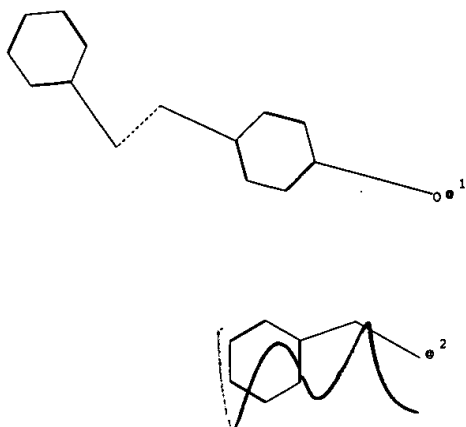
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G1:O,S,N

G2:[*1],[*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 15:CLASS 16:Atom 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom
24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:CLASS 31:CLASS 32:CLASS
33:CLASS 34:Atom 35:Atom 36:Atom 37:Atom 38:Atom 39:Atom 43:CLASS 44:CLASS



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normalized bonds :

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33:CLASS 34:Atom 35:Atom 36:Atom 37:Atom 38:Atom 39:Atom 43:CLASS 44:CLASS